## Quick definitions (Thimerosal)

• noun: a light-colored crystalline powder (trade name Merthiolate) used as a surgical antiseptic

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AIDS Alert. 1999 Feb;14(2):suppl 3-4.

Related Articles, Links

## 'Ideal' microbicide may be best form of protection.

[No authors listed]

AIDS: AIDS vaccines are a long way from being commercially available, however, microbicides may be a viable way to help prevent HIV transmission. In several observational studies microbicides have performed well, but in two controlled studies there was no decrease in infection rates. Nonoxynol-9 (N-9) may be able to kill pathogens such as HIV and other sexually transmitted diseases, although there have been difficulties in administering the right dosage. A low dose is ineffective, and a high dose causes irritation that can leave a woman at higher risk for contracting the disease. Other microbicide products under development are discussed.

Publication Types:

• Newspaper Article

PMID: 11366179 [PubMed - indexed for MEDLINE]

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Curr Pharm Des. 2004;10(3):315-36.

Related Articles, Links

## Clinical development of microbicides for the prevention of HIV infection.

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The HIV/AIDS pandemic continues its spread at a rate of over 15,000 new infections every day. Sexual transmission of HIV-1 is the dominant mode of this pandemic spread. For the first time since the disease emerged in the early 1980s, about half the 42 million people now living with HIV/AIDS worldwide are women. Worldwide, more than 90 percent of all adolescent and adult HIV infections have resulted from heterosexual intercourse. The "feminization" of the pandemic largely driven by the social, economic, and biological factors warrants urgent attention particularly for the adolescent female population. In the absence of an effective prophylactic anti-HIV therapy or vaccine, current efforts are aimed at developing intravaginal/intrarectal topical formulations of anti-HIV agents or microbicides to curb the mucosal and perinatal HIV transmission. Microbicides would provide protection by directly inactivating HIV or preventing HIV from attaching, entering or replicating in susceptible target cells as well as dissemination from target cells present in semen or the host cells that line the vaginal/rectal wall. Thus, ideally, anti-HIV microbicides should be capable of attacking HIV from different angles. In addition, a contraceptive microbicide could help prevent unintended pregnancies worldwide. To be a microbicide, these agents must be safe, effective following vaginal or rectal administration, and should cause minimal or no genital symptoms following long-term repeated usage. A safe and efficacious anti-HIV microbicide is not yet available despite the fact that more than 60 candidate agents have been identified to have in vitro activity against HIV, 18 of which have advanced to clinical testing. Targeting HIV entry has been a favored approach because it is the first step in the process of infection and several readily available anionic polymeric products seem to variably interfere with these processes are the primary candidates for potential microbicides. Formulations of some anionic polymeric antiviral agents have been tested at various doses and various durations for safety, tolerability, and acceptability in Phase I/II clinical trials (vaginal, rectal, or penile studies) in HIV-uninfected and/or HIV-infected populations. Current multicenter Phase I/II safety and Phase II/III efficacy studies that are being conducted or planned in different geographical locations by various special interest groups are designed for rapid clinical development of candidate products. The currently marketed detergent-type spermicide, nonoxynol-9 (N-9), has failed in Phase III clinical trials, due to the drug-induced formation of localized genital lesions that might in fact actually promote virus transmission. Alternative "first-generation" microbicides that have undergone Phase I/II safety and tolerability studies in HIV-uninfected and/or HIV-infected volunteers include polymeric viral fusion inhibitors (dextrin sulfate/Emmelle, carrageenans [PC-213, PC-503, PC-515/Carraguard], cellulose sulfate/Ushercell, polystyrene sulfonate, naphthalene sulfonate [PIC 024-4/PRO 2000/5], acidifying gel [Carbomer 974P/BufferGel], Lactobacillus (L. crispatus) suppository/CTV-05\_detergent-type dual-function barriers [ACIDFORM, GEDA Plus, SURETE, Glyminox/C31G/Savvy, Invisible Condom], herbal extracts [Praneem], and viral replication inhibitors [PMPA/Tenofovir]. For majority of these products, no information is available regarding their long-term mucosal safety, carcinogenicity potential, bioavailability, or efficacy following their extended vaginal or rectal exposure. The irritative genitourinary symptoms reported for a number of these first-generation products in Phase I clinical trials implies that the "soft" preclinical endpoints for mucosal safety established for the use and development of vaginal spermicides may not be rigorous enough for vaginal and rectal microbicides because of the efficient sexual tra virus diversity, and genetic environment. It is now apparent that sexually

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transmitted R5 HIV-1 viruses have less positive charge on their surface compared with the R4 HIV-1 viruses, which may limit the anionic polymers as topical microbicides despite extensive clinical trials. Nevertheless, their ongoing clinical trials, reviewed here, using optimized formulations, and special populations in various geographic locations are paving the way for future rigorous clinical testing of "mechanism-based" broad-spectrum anti-HIV microbicides that are currently under intense development. It is anticipated that future microbicide trials will focus on combination of products capable of attacking HIV life cycle at multiple steps intended to increase efficacy, limit cross-resistance as well as minimize microbicide-induced host toxicity.

**Publication Types:** 

- Review
- Review, Tutorial

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